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(54) Title: ORAL COMPOSITIONS EFFECTIVE AGAINST PLAQUE AND GINGIVITIS (57) Abstract Disclosed are oral compositions which are effective against plaque and gingivitis and contain a noncationic water insoluble antibacterial agent.		

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ORAL COMPOSITIONS EFFECTIVE AGAINST PLAQUE AND GINGIVITIS

Douglas Charles Mohl

TECHNICAL FIELD

5 The present invention relates to oral compositions which provide antiplaque and antigingivitis benefits as well as being effective against other anaerobic infections of the mouth.

10 Plaque induced diseases, including periodontitis and gingivitis, are believed to involve anaerobic bacterial infections. Periodontal disease affects the periodontium, which is the investing and supporting tissue surrounding a tooth (i.e., the periodontal ligament, the gingiva, and the alveolar bone). Gingivitis and periodontitis are inflammatory disorders of the gingiva and the periodontal ligament, respectively. Gingivitis and periodontitis are more severe conditions involving
15 degenerative disorders of the tissue. Combinations of inflammatory and degenerative conditions are termed periodontitis complex.

20 Periodontal disease is a major cause of tooth loss in adults. Tooth loss from periodontal disease is a significant problem beginning at age 35, but even by age 15 it is estimated that about 4 out of 5 persons already have gingivitis and 4 out of 10 have periodontitis.

25 While good oral hygiene, as achieved by brushing the teeth with a cleansing dentifrice, may help reduce the incidence of periodontal disease, it does not necessarily prevent or eliminate its occurrence. This is because microorganisms contribute to both the initiation and progress of periodontal disease. Thus, in order to prevent or treat periodontal disease, these microorganisms must be suppressed by some means other than simple
30 mechanical scrubbing. Towards this end, there has been a great deal of research aimed at developing therapeutic dentifrices, mouthwashes, and methods of treating periodontal disease which are effective in suppressing these microorganisms.

35 The use of noncationic, water-insoluble antibacterial agents in oral products is disclosed in a number of references. One such reference is U.S. Patent 4,022,889 to Vinson et al. Vinson describes compositions containing zinc salts and antibacterial agents such as halogenated salicylanilides and halogenated hydroxydiphenyl ethers.

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Another reference disclosing noncationic water-insoluble antibacterial agents is U.K. Patent Application GB 2,200,551, published August 10, 1988. In addition to the antibacterial, the compositions contain a molecularly dehydrated polyphosphate salt. The salt is stated to improve the effectiveness of the antibac-

Still another reference disclosing such antibacterials combined with polyethylene glycols in oral compositions is European Patent Application 02,220,890, May 6, 1987. All prior art references are incorporated herein by reference in total.

It has now been found that the bioavailability and effectiveness of the antibacterial can be improved by incorporating the antibacterial, a linear anionic polycarboxylate and a polyethylene glycol into the composition.

It is therefore an object of the present invention to provide improved oral care products containing specific antibacterial agents.

It is a further object of the present invention to provide more effective products for treating diseases of the oral cavity.

It is still a further objective to provide methods for treating diseases of the oral cavity.

These and other objects will become readily apparent from the detailed disclosure which follows.

All percentages and ratios used herein are by weight unless otherwise specified. Also, all measurements referred to herein are made at 25°C in the composition unless otherwise specified.

SUMMARY OF THE INVENTION

The present invention, in certain aspects, embraces oral care product containing water-insoluble, noncationic antibacterial agents, a polyethylene glycol solvent and an anionic linear, polycarboxylate.

The present invention also encompasses a method for treating diseases of the oral cavity using noncationic water insoluble antibacterial agents.

By "oral compositions" as used herein means a product which in the ordinary course of usage is not intentionally swallowed for

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purposes of systemic administration of particular therapeutic agents, but is rather retained in the oral cavity for a time sufficient to contact substantially all of the dental surfaces and/or oral tissues for purposes of oral activity.

5 By "safe and effective amount" as used herein means sufficient amount of material to provide the desired benefit while being safe to the hard and soft tissues of the oral cavity.

By the term "comprising", as used herein, is meant that various additional components can be conjointly employed in the compositions of this invention as long as the listed materials perform their intended functions.

By the term "carrier", as used herein, is meant a suitable vehicle which is pharmaceutically acceptable and can be used to apply the present compositions in the oral cavity.

15 DETAILED DESCRIPTION OF THE INVENTION

The present invention in certain aspects involves the use of water-insoluble, noncationic antibacterials with a polyethylene glycol solvent and a carboxyvinyl polymer having molecular weight of 3,000,000 or greater. The essential and optional components of the compositions are made using the process described in detail below.

Antibacterial Agents

Given below are examples of antibacterial agents useful in the compositions of the present invention which are water insoluble and noncationic.

Halogenated Diphenyl Ethers

2',4,4'-trichloro-2-hydroxy-diphenyl ether (Triclosan)
2,2'-dihydroxy-5,5'-dibromo-diphenyl ether.

30 Phenolic Compounds (including phenol and its homologs, mono- and poly-alkyl and aromatic halophenols, resorcinol and its derivatives, bisphenolic compounds and halogenated salicylanilides).

Phenol and its Homologs

Phenol

35 2 Methyl	- Phenol
3 Methyl	- Phenol
4 Methyl	- Phenol
4 Ethyl	- Phenol
2,4-Dimethyl	- Phenol

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	2,5-Dimethyl	- Phenol
	3,4-Dimethyl	- Phenol
	2,6-Dimethyl	- Phenol
	4-n-Propyl	- Phenol
5	4-n-Butyl	- Phenol
	4-n-Amyl	- Phenol
	4-tert-Amyl	- Phenol
	4-n-Hexyl	- Phenol
	4-n-Heptyl	- Phenol
10	<u>Mono- and Poly-Alkyl and Aromatic Halophenols</u>	
	p-Chlorophenol	
	Methyl	- p-Chlorophenol
	Ethyl	- p-Chlorophenol
	n-Propyl	- p-Chlorophenol
15	n-Butyl	- p-Chlorophenol
	n-Amyl	- p-Chlorophenol
	sec-Amyl	- p-Chlorophenol
	n-Hexyl	- p-Chlorophenol
	Cyclohexyl	- p-Chlorophenol
20	n-Heptyl	- p-Chlorophenol
	n-Octyl	- p-Chlorophenol
	o-Chlorophenol	
	Methyl	- o-Chlorophenol
	Ethyl	- o-Chlorophenol
25	n-Propyl	- o-Chlorophenol
	n-Butyl	- o-Chlorophenol
	n-Amyl	- o-Chlorophenol
	tert-Amyl	- o-Chlorophenol
	n-Hexyl	- o-Chlorophenol
30	n-Heptyl	- o-Chlorophenol
	o-Benzyl	- p-Chlorophenol
	o-Benxyl-m-methyl	- p-Chlorophenol
	o-Benzyl-m, m-dimethyl	- p-Chlorophenol
	o-Phenylethyl	- p-Chlorophenol
35	o-Phenylethyl-m-methyl	- p-Chlorophenol
	3-Methyl	- p-Chlorophenol
	3,5-Dimethyl	- p-Chlorophenol
	6-Ethyl-3-methyl	- p-Chlorophenol
	6-n-Propyl-3-methyl	- p-Chlorophenol

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	6-iso-Propyl-3-methyl	- p-Chlorophenol
	2-Ethyl-3,5-dimethyl	- p-Chlorophenol
	6-sec-Butyl-3-methyl	- p-Chlorophenol
	2-iso-Propyl-3,5-dimethyl	- p-Chlorophenol
5	6-Diethylmethyl-3-methyl	- p-Chlorophenol
	6-iso-Propyl-2-ethyl-3-methyl	- p-Chlorophenol
	2-sec-Amyl-3,5-dimethyl	- p-Chlorophenol
	2-Diethylmethyl-3,5-dimethyl	- p-Chlorophenol
	6-sec-Octyl-3-methyl	- p-Chlorophenol
10	p-Bromophenol	
	Methyl	- p-Bromophenol
	Ethyl	- p-Bromophenol
	n-Propyl	- p-Bromophenol
	n-Butyl	- p-Bromophenol
15	n-Amyl	- p-Bromophenol
	sec-Amyl	- p-Bromophenol
	n-Hexyl	- p-Bromophenol
	cyclohexyl	- p-Bromophenol
	o-Bromophenol	
20	tert-Amyl	- o-Bromophenol
	n-Hexyl	- o-Bromophenol
	n-Propyl-m,mDimethyl	- o-Bromophenol
	2-Phenyl Phenol	
	4-Chloro-2-methyl phenol	
25	4-Chloro-3-methyl phenol	
	4-Chloro-3,5-dimethyl phenol	
	2,4-dichloro-3,5-dimethylphenol	
	3,4,5,6-terabromo-2-methylphenol	
	5-methyl-2-pentylphenol	
30	4-isopropyl-3-methylphenol	
	5-Chloro-2-hydroxydiphenylmethane	
	<u>Resorcinol and its Derivatives</u>	
	Resorcinol	
	Methyl	- Resorcinol
35	Ethyl	- Resorcinol
	n-Propyl	- Resorcinol
	n-Butyl	- Resorcinol
	n-Amyl	- Resorcinol
	n-Hexyl	- Resorcinol

	n-Heptyl	- Resorcinol
	n-Octyl	- Resorcinol
	n-Nonyl	- Resorcinol
	Phenyl	- Resorcinol
5	Benzyl	- Resorcinol
	Phenylethyl	- Resorcinol
	Phenylpropyl	- Resorcinol
	p-Chlorobenzyl	- Resorcinol
	5-Chloro	-2,4-Dihydroxydiphenyl Methane
10	4'-Chloro	-2,4-Dihydroxydiphenyl Methane
	5-Bromo	-2,4-Dihydroxydiphenyl Methane
	4'-Bromo	-2,4-Dihydroxydiphenyl Methane

Bisphenolic Compounds

	2,2'-methylene bis (4-chlorophenol)
15	2,2'-methylene bis (3,4,6-trichlorophenol)
	2,2'-methylene bis (4-chloro-6-bromophenol)
	bis (2-hydroxy-3,5-dichlorophenyl) sulphide
	bis (2-hydroxy-5-chlorobenzyl) sulphide

Halogenated Salicylanilides

20	4',5-dibromosalicylanilide
	3,4',5-trichlorosalicylanilide
	3,4',5-tribromosalicylanilide
	2,3,3',5-tetrachlorosalicylanilide
	3,3',5-trichlorosalicylanilide
25	3,5-dibromo-3'-trifluoromethyl salicylanilide
	5-n-octanoyl-3'-trifluoromethyl salicylanilide
	3,5-dibromo-4'-trifluoromethyl salicylanilide
	3,5-dibromo-3'-trifluoromethyl salicylanilide

(Fluorophene)

30 Benzoic Esters

p-Hydroxybenzoic Acid

	Methyl	- p-Hydroxybenzoic Acid
	Ethyl	- p-Hydroxybenzoic Acid
	Propyl	- p-Hydroxybenzoic Acid
35	Butyl	- p-Hydroxybenzoic Acid

Halogenated Carbanilides

	3,4,4'-trichlorocarbanilide
	3-trifluoromethyl-4,4'-dichlorocarbanilide
	3,3',4-trichlorocarbanilide

5 The antibacterial agent is present in the oral compositions of the present invention in an effective antiplaque amount, typically about 0.01-5% by weight, preferably about 0.03-1%. The antibacterial agent is substantially water-insoluble, meaning that its solubility is less than about 1% by weight in water at 25°C and may be even less than about 0.1%. If an ionizable group is present solubility is determined at a pH at which ionization does not occur.

Polyethylene Glycols

10 The polyethylene glycols useful in this invention can be any of a wide range of molecular weights such as from about 100 to about 1,000, preferably from about 300 to about 600. The glycol is present in an amount of from about 1% to about 10%, preferably from about 3% to about 6%.

Anionic Linear Polycarboxylate

15 The anionic polymeric polycarboxylates employed herein are well known, being employed in the form of their free acids or partially or preferably fully neutralized water soluble alkali metal (e.g. potassium and preferably sodium) or ammonium salts. Preferred are 1:4 to 4:1 copolymers of maleic anhydride or acid with another polymerizable ethylenically unsaturated monomer, preferably methyl vinyl ether (methoxyethylene) having a molecular weight (M.W.) of about 30,000 to about 1,000,000. These copolymers are available for example as Gantrez (AN 139(M.W. 500,000), A.N. 119 (M.W. 250,000) and preferably S-97 Pharmaceutical Grade (M.W. 70,000), of GAF Corporation.

20 Other operative polymeric polycarboxylates include those such as the 1:1 copolymers of maleic anhydride with ethyl acrylate, hydroxyethyl methacrylate, N-vinyl-2-pyrrolidone, or ethylene, the latter being available for example as Monsanto EMA No. 1103, M.W. 10,000 and EMA Grade 61, and 1:1 copolymers of acrylic acid with methyl or hydroxyethyl methacrylate, methyl or ethyl acrylate, isobutyl vinyl ether or N-vinyl-2-pyrrolidone.

35 Additional operative polymeric polycarboxylates disclosed in above referred to U.S. Patent Nos. 4,138,477 and 4,183,914, incorporated herein by reference, include copolymers of maleic anhydride with styrene, isobutylene or ethyl vinyl ether, polyacrylic, polyitaconic and polymaleic acids, and sulfoacrylic oligomers of M.W. as low as 1,000 available as Uniroyal ND-2.

Suitable generally are polymerized olefinically or ethylenically unsaturated carboxylic acids containing an activated carbon-to-carbon olefinic double bond and at least one carboxyl group, that is, an acid containing an olefinic double bond which readily functions in polymerization because of its presence in the monomer molecule either in the alpha-beta position with respect to a carboxyl group or as part of a terminal methylene grouping. Illustrative of such acids are acrylic, methacrylic, ethacrylic, alpha-chloroacrylic, crotonic, beta-acryloxy propionic, sorbic, alpha-chlorsorbic, cinnamic, beta-styrylacrylic, muconic, itaconic, citraconic, mesaconic, glutaconic, aconitic, alpha-phenylacrylic, 2-benzyl acrylic, 2-cyclohexylacrylic, angelic, umbellic, fumaric, maleic acids and anhydrides. Other different olefinic monomers copolymerizable with such carboxylic monomers include vinylacetate, vinyl chloride, dimethyl maleate and the like. Copolymers contain sufficient carboxylic salt groups for water-solubility.

The linear anionic polymeric polycarboxylate component is mainly a hydrocarbon with optional halogen and O-containing substituents and linkages as present in for example ester, ether and OH groups, and when present is generally employed in the instant compositions in approximate weight amounts of 0.05 to 3%, preferably 0.05 to 2%, more preferably 0.1 to 2%.

Water

Water is another essential component of this invention. Water employed in the preparation of commercially suitable compositions should preferably be deionized and free of organic impurities. Water generally comprises from about 10% to 50%, preferably from about 20% to 40%, by weight of the toothpaste compositions herein while mouthwashes contain from about 40% to about 95%. These amounts of water include the free water which is added plus that which is introduced with other materials as with sorbitol.

Optional Components

The compositions of the present invention may contain in addition to the above-listed components many others which will be somewhat dependent on the type of composition (mouthwashes, toothpastes, topical gels, prophylaxis pastes and the like). Toothpastes and mouthwashes are the preferred systems with

toothpastes being the most preferred.

5 Toothpastes contain as a major component an abrasive. The abrasive polishing material contemplated for use in the present invention can be any material which does not excessively abrade
10 dentin. These include, for example, silicas including gels and precipitates, calcium carbonate, dicalcium orthophosphate dihydrate, calcium pyrophosphate, tricalcium phosphate, calcium polymetaphosphate, insoluble sodium polymetaphosphate, hydrated alumina, and resinous abrasive materials such as particulate
15 condensation products of urea and formaldehyde, and others such as disclosed by Cooley et al. in U.S. Patent 3,070,510, December 25, 1962, incorporated herein by reference. Mixtures of abrasives may also be used.

15 Silica dental abrasives, of various types, can provide the unique benefits of exceptional dental cleaning and polishing performance without unduly abrading tooth enamel or dentin. Silica abrasive materials are also exceptionally compatible with sources of soluble fluoride and other ion sources. For these reasons they are preferred for use herein.

20 The silica abrasive polishing materials useful herein, as well as the other abrasives, generally have an average particle size ranging between about 0.1 and 30 microns, preferably 5 and 15 microns. The silica abrasive can be precipitated silica or silica
25 gels such as the silica xerogels described in Pader et al., U.S. Patent 3,538,230, issued March 2, 1970 and DiGiulio, U.S. Patent 3,862,307, June 21, 1975, both incorporated herein by reference. Preferred are the silica xerogels marketed under the tradename "Syloid" by the W.R. Grace & Company, Davison Chemical Division. Preferred precipitated silica materials include those marketed by
30 the J.M. Huber Corporation under the tradename, "Zeodent", particularly the silica carrying the designation "Zeodent 119". These silica abrasive are described in U.S. Patent 4,340,583, July 29, 1982, incorporated herein by reference.

35 The abrasive in the toothpaste compositions described herein is present at a level of from about 6% to about 70%, preferably from about 15% to about 30%.

Flavoring agents, as was noted earlier, can also be added to the dentifrice and other compositions of the present invention. Suitable flavoring agents include oil of wintergreen, oil of

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peppermint, oil of spearmint, oil of sassafras, and oil of clove. Sweetening agents are also useful and include aspartame, acesulfame, saccharin, dextrose, levulose and sodium cyclamate. Flavoring and sweetening agents are generally used in the compositions herein at levels of from about 0.005% to about 2% by weight and may be used as a solvent for the antibacterials hereinbefore indicated.

In preparing toothpastes, it is necessary to add some thickening material to provide a desirable consistency. Preferred thickening agents are carboxyvinyl polymers, carrageenan, hydroxyethyl cellulose and water soluble salts of cellulose ethers such as sodium carboxymethyl cellulose and sodium carboxymethyl hydroxyethyl cellulose. Natural gums such as gum karaya, gum arabic, and gum tragacanth and polysaccharide gums such as xanthan gum can also be used. Colloidal magnesium aluminum silicate or finely divided silica can be used as part of the thickening agent to further improve texture. Thickening agents in an amount from 0.05% to 1.5% by weight of the total composition may be used.

It is also desirable to include a humectant in a toothpaste to keep it from hardening. Suitable humectants include glycerin, sorbitol, and other edible polyhydric alcohols at a combined level of from about 10% to about 70%.

Another preferred embodiment of the present invention is a mouthwash composition. Mouthwashes generally comprise from about 20:1 to about 2:1 of a water/ethyl alcohol solution and preferably other ingredients such as flavor, sweeteners, humectants and sudsing agents such as those described above. The humectants, such as glycerin and sorbitol give a moist feel to the mouth. Generally, on a weight basis the mouthwashes of the invention comprise 5% to 60% (preferably 10% to 25%) ethyl alcohol, 0% to 20% (preferably 5% to 20%) of a humectant, 0% to 2% (preferably 0.01% to 0.5%) emulsifying agent, 0% to 0.5% (preferably 0.005% to 0.06%) sweetening agent such as saccharin, 0% to 0.3% (preferably from 0.03% to 0.3%) flavoring agent, and the balance water.

Another optional component is a fluoride ion source. The sources of fluoride ions, or fluoride-providing compounds, are well known in the art as anticaries agents and also act as such agents in the practice of this invention as well as to inhibit pyrophosphatase. These compounds may be slightly soluble in water

or may, preferably, be fully water-soluble. They are characterized by their ability to release fluoride ions in water and by freedom from undesired reaction with other compounds of the oral preparation. Among these materials are inorganic fluoride salts, such as soluble alkali metal, alkaline earth metal salts, for example, sodium fluoride, barium fluoride, sodium fluorsilicate, ammonium fluorosilicate, sodium fluorozirconate, sodium monofluorophosphate, aluminum mono- and di-fluorophosphate, and fluorinated sodium calcium pyrophosphate. Alkali metal and tin fluorides, such as sodium and stannous fluorides, sodium monofluorophosphate (MFP) and mixtures thereof, are preferred.

The amount of fluoride-providing compound is dependent to some extent upon the type of compound, its solubility, and the type of oral preparation, but it must be a nontoxic amount, generally about 0.005 to about 3.0% in the preparation. In a dentifrice preparation, e.g. dental gel, toothpaste (including cream), an amount of such compound which releases up to about 5,000 ppm of F ion by weight of the preparation is considered satisfactory. Any suitable minimum amount of such compound may be used, but it is preferable to employ sufficient compound to release about 300 to 2,000 ppm, more preferably about 800 to about 1,500 ppm of fluoride ion. Typically, in the cases of alkali metal fluorides and stannous fluoride, this component is present in an amount up to about 2% by weight, based on the weight of the preparation, and preferably in the range of about 0.05% to 1%. In the case of sodium monofluorophosphate, the compound may be present in an amount of about 0.1-3%, more typically about 0.76%.

Still another optional component for use in the compositions of the present invention is an anticalculus agent. These agents include any which are effective against calculus such as pyrophosphate salts as disclosed in U.S. Patent 4,515,772, May 7, 1985 incorporated herein by reference. The preferred agents are mono, di, tri and tetra alkali metal and ammonium pyrophosphate. Such agents are used in amounts sufficient to reduce calculus. These amounts are preferably in an amount of at least about 1% P₂O₇, most preferably at least about 1.3%, most preferably at least about 1.5%.

Other anticalculus agents are metal ions such as zinc disclosed in U.S. Patent 4,022,880, May 10, 1977 to Vinson

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incorporated herein by reference. Still others are polymers such as those described in U.S. Patent 4,661,341, April 28, 1987 to Benedict and U.S. Patent 3,429,963, February 25, 1969 to Shedlovsky, both of which are incorporated herein by reference. Such metals are used in an amount of from about 0.05% to about 5%, preferably about 0.5% to about 2%, while such polymers are used in amounts of from about 0.01% to about 10%, preferably from about 0.1% to about 5%.

Surfactants are also useful in the composition of this invention include many different materials. Suitable surfactants include any which are reasonably stable and function over a wide pH range. Included are non-soap anionic, nonionic, cationic, zwitterionic and amphoteric organic synthetic surfactants. Many of these are disclosed by Gieske et al. in U.S. Patent 4,051,234, September 27, 1988 incorporated herein in total by reference.

Preferred surfactants include alkyl sulfates. Any surfactant used is at a level of from about 0.2% to about 6%, preferably from about 0.6% to about 2% in a toothpaste and from about 0.01% to about 5%, preferably from about 0.1% to about 0.5% in a mouthwash.

The pH of the present compositions and/or its pH in the mouth can be any pH which is safe for the mouth's hard and soft tissues. Such pH's are generally from about 3 to about 10, preferably from about 4 to about 9.

Given below are non-limiting examples which illustrate the compositions of the present invention.

EXAMPLES I - IV

Given below are four examples of compositions.

<u>Component</u>		<u>Weight %</u>			
		(I)	(II)	(III)	(IV)
30	Water	20.518	20.518	14.069	11.165
	Sorbitol (70%)	26.600	24.583	30.000	51.652
	Glycerin	8.000	8.000	8.000	-
	Sodium fluoride	0.243	0.243	0.321	0.243
	Sodium acid pyrophosphate	1.650	1.650	1.650	-
	Tetrasodium pyrophosphate	2.160	2.160	2.160	-
	Tetrapotassium pyrophosphate	5.379	7.379	6.800	-
	(60-65%)				
35	Monosodium phosphate	-	-	-	0.590
	Trisodium phosphate	-	-	-	1.450
	Saccharin	0.470	0.470	0.300	0.300
	FD&C Blue No. 1	-	-	-	0.050
	Titanium dioxide	0.500	0.500	0.700	0.525
	Flavor	1.100	1.100	0.970	0.970
	PEG-300	4.000	4.000	4.000	4.000

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	Triclosan	0.280	0.450	0.280	0.280
	Sodium alkyl sulfate (27.9% aqueous solution)	6.000	6.000	6.000	6.000
	Silica	20.300	20.300	22.000	20.000
	Xanthan gum	0.600	0.600	0.500	0.475
	Carbomer 956	0.200	0.200	0.250	0.300
5	Gantrez M-957	<u>2.000</u>	<u>2.000</u>	<u>2.000</u>	<u>2.000</u>
		100.000	100.000	100.000	100.000

EXAMPLES V - VI

	<u>Component</u>	<u>Weight %</u>	
	Ethanol	10	15
10	PEG-300	4	6
	Flavor	0.1	0.15
	Triclosan	0.03	0.03
	Sodium Alkyl Sulfate (27.9%)	1.6	1.8
	Sorbitol	10	15
	Glycerin	10	10
	Gantrez M-957	2	2.5
15	Water	q.s. 100	q.s. 100

The above compositions are made in a conventional manner.

The performance of the above compositions of this present invention are superior due to the improved bioavailability of the triclosan antibacterial.

WHAT IS CLAIMED:

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1. An oral composition comprising a noncationic water insoluble antibacterial, a polyethylene glycol solvent, a linear anionic polycarboxylate and water.
2. A composition according to Claim 1 wherein said antibacterial is a phenolic compound.
3. A composition according to either of Claims 1 or 2 wherein said polyethylene glycol has a molecular weight of from about 100 to about 1,000.
4. A composition according to any of Claims 1-3 wherein said polycarboxylate is an acrylic acid polymer.
5. A composition according to any of Claims 1-4 wherein said polymer is a copolymer of vinyl methyl ether and maleic anhydride.
6. A composition according to any of Claims 1-5 wherein said composition is a toothpaste or a mouthwash.
7. A composition according to any of Claims 1-6 wherein said composition is a toothpaste which in addition contains an abrasive and a binder.
8. A composition according to any of Claim 1-7 wherein said toothpaste also contains triclosan as the antibacterial agent.
9. A composition according to any of Claims 1-8 wherein said toothpaste contains a soluble fluoride ion source.
10. A composition according to any of Claims 1-9 wherein said toothpaste contains an anticalculus agent.
11. A composition according to any of Claims 1-10 wherein said anticalculus agent is a soluble pyrophosphate salt.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 91/09377

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)⁶

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 A61K7/16

II. FIELDS SEARCHEDMinimum Documentation Searched⁷

Classification System	Classification Symbols
Int.Cl. 5	A61K

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are included in the Fields Searched⁸**III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹**

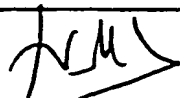
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	GB,A,2 200 551 (COLGATE-PALMOLIVE) 10 August 1988 cited in the application see page 22, line 12 - line 23; claims 1-33; table 3	1-11
X	FR,A,2 641 186 (COLGATE-PALMOLIVE) 6 July 1990 cited in the application see page 23, line 16 - page 24, line 4; claims 1-40; examples 1,2	1-10

¹⁰ Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "T" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "A" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search 26 MAY 1992	Date of Mailing of this International Search Report 12.06.92
International Searching Authority EUROPEAN PATENT OFFICE	Signature of Authorized Officer WILLEKENS 

Form PCT/ISA/210 (second sheet) (January 1985)

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. US 9109377
SA 55886**

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB-A-2200551	10-08-88	AU-B- 615173	26-09-91
		AU-A- 1017588	04-08-88
		AU-A- 7423591	11-07-91
		AU-A- 7423691	11-07-91
		AU-A- 7423891	11-07-91
		BE-A- 1001110	18-07-89
		DE-A- 3802168	11-08-88
		FR-A- 2610195	05-08-88
		FR-A- 2640134	15-06-90
		FR-A- 2647013	23-11-90
		FR-A- 2647010	23-11-90
		FR-A- 2647011	23-11-90
		GB-A, B 2230187	17-10-90
		GB-A, B 2230188	17-10-90
		GB-A, B 2230189	17-10-90
		JP-A- 63258404	25-10-88
		NL-A- 8800206	16-08-88
		SE-A- 8800299	31-07-88
		US-A- 4894220	16-01-90
		US-A- 5043154	27-08-91
		US-A- 5037635	06-08-91
		US-A- 5037637	06-08-91
		US-A- 5080887	14-01-92
FR-A-2641186	06-07-90	US-A- 4894220	16-01-90
		US-A- 5032386	16-07-91
		AU-A- 4676889	05-07-90
		AU-A- 4676989	05-07-90
		CA-A- 2006703	29-06-90
		CA-A- 2006706	29-06-90
		CA-A- 2006713	29-06-90
		CA-A- 2006716	29-06-90
		CA-A- 2006717	29-06-90
		CA-A- 2006719	29-06-90
		CH-A- 679741	15-04-92
		CH-A- 679639	31-03-92
		DE-A- 3942642	30-08-90
		DE-A- 3942643	05-07-90
		FR-A- 2641187	06-07-90
		GB-A- 2227660	08-08-90

EPO FORM P007

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US 9109377
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The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 26/05/92

Page 2

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A-2641186		GB-A- 2227661	08-08-90
		JP-A- 2288819	28-11-90
		JP-A- 2288820	28-11-90
		LU-A- 87650	10-07-90
		LU-A- 87652	15-05-90
		NL-A- 8903186	16-07-90
		NL-A- 8903187	16-07-90
		SE-A- 8904179	30-06-90
		SE-A- 8904180	30-06-90
		AU-A- 4677189	28-02-91
		CA-A- 2006707	25-02-91
		CH-A- 679674	31-03-92
		CN-A- 1049669	06-03-91
		DE-A- 3942641	28-02-91
		FR-A- 2651235	01-03-91
		GB-A- 2235201	27-02-91
		JP-A- 3083910	09-04-91
		NL-A- 8903188	18-03-91
		AU-A- 4676689	28-02-91
		CA-A- 2006718	25-02-91
		CN-A- 1049606	06-03-91
		DE-A- 3942644	28-02-91
		FR-A- 2651124	01-03-91
		GB-A- 2235133	27-02-91
		JP-A- 3083911	09-04-91
		LU-A- 87651	15-05-90
		NL-A- 8903185	18-03-91
		SE-A- 8904181	26-02-91

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